BSC Study Nomination Review

Meeting of the National Toxicology Program
Board of Scientific Counselors

National Institute of Environmental Health Sciences
Rall Building, Rodbell Conference Center
Research Triangle Park, NC

December 6, 2007

NTP Study Nomination: Nanoscale Gold

NTP Staff Scientist: Dr. Nigel Walker t: (919) 541-4893

BSC Reviewer: Dr. Jim Riviere

Ad Hoc reviewer: Dr. Stephen Roberts

1. Is a clear and valid rationale for the proposed research program articulated in the NTP research concept document?

Yes. There is a strong need to define basic ADME parameters as a function of size and coating, as well as to define fundamental toxicology protocols and characterization metrics for assessing safety of nanomaterials that are presently in commerce or are proposed to serve as platforms for future therapeutics. This rationale was clearly articulated in this nomination. The use of nanogold as platforms for therapeutics further underscores a need for basic ADME and toxicology to be defined.

2. Is the proposed research program as outlined in the research concept document appropriate in scope given the public health importance of the issue or substance proposed for study? Are there other studies that should be considered as part of this research program?

The proposed research program's overall scope is adequately presented. However, the exact experiments are not presented in sufficient detail to critically assess several experimental design factors. One concern is how knowledge gained from other NTP nanoscale research projects (e.g. nanosilver) will be integrated into the design of the present studies. There was consensus among reviewers and BSC members that three gold particles are not sufficient to shed light on both particle size and surface characteristics, as results would be confounded (e.g. surface interactions between particles overwhelm size effects within a particle type). Some discussion occurred whether soluble gold studies should also be conducted as a control, and whether a neutral nanoparticle (e.g. fullerenes) be considered as an additional control for bridging data between experiments of different particle compositions.

It is crucial that multiple characterization techniques be conducted and that particle dose and numbers be carefully measured and controlled as additional studies are conducted. Approaches for analyzing such data (e.g. dose that is a distribution of different particle sizes) need to be developed and defined, or at least the data collected with sufficient granularity that post-hoc analyses could be conducted. One written public comment raised the question of whether such studies should be conducted before characterization techniques are fully accepted.. However, "proper" characterization metrics will never be defined unless studies such as proposed here are conducted to determine which are biologically relevant.

A strength of the proposed studies would be to use standard particles so that results can be tied to work of other investigators. Use of NIST standard particles would make these same materials available for other researchers outside of NTP to employ in their research.

3. Does the proposed research program address an important area of biomedical research (e.g. children's health, genetic susceptibility, specific environmental disease) and/or advance the field of environmental health sciences?

Yes. Nanoscale materials are presently entering commerce without adequate standards being set for evaluating their safety. It is crucial that research be conducted to define the basic approaches to doing nanotoxicology studies. A number of BSC members stressed that the definition of proper dosimetry metrics including surface are, coatings and size distributions would advance the field of nanotoxicology.

4. Does the proposed research program merit utilization of NTP resources, and if so, what priority (low, moderate, or high) should it be given?

High

Reviewer's Signature: _____ Date: _____